REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative at (858) 720-5133.

Status of the Claims

Pending and withdrawn claims

Claims 8 to 28, 30, 31, 33 to 41, 44, 46, 48 to 59, 64 and 66 to 72 are pending. Claims 8 to 14, 19 to 28, 30, 31, 33 to 41, 44, 46, 48 to 58, 64 and 66 to 68, 71 and 72 are pending and under consideration. Claims 15 to 18, 59, 69 and 70 are withdrawn.

Outstanding Rejections

Claims 8 to 11, 19, 23 to 28, 30, 31, 33 to 41, 46, 48, 50 to 53, 56, 57, 64, 67, 68, 71 and 72 stand rejected as allegedly failing to comply with the requirements of 35 U.S.C. §112, second paragraph. The rejection of claims 8 to 11, 19, 23 to 28, 30, 31, 33 to 41, 46, 48, 50 to 53, 56, 57 and 64, under section 112, first paragraph, is maintained. Claims 8 to 11, 13, 19, 23 to 28, 30, 31, 33 to 40, 50 to 53, 56, 57 and 64 remain rejected, and claims 67 and 68 are newly rejected, under 35 USC §103(a) as allegedly unpatentable over Cheng, et al., U.S. Patent No. 5,939,303, filed November 6, 1996, issued August 17, 1999 (hereinafter "Cheng"), in view of Greiner et al. (1993) Archives of Biochemistry and Biophysics 303:107-113 (hereinafter "Greiner")Claims 8 to 13, 19, 24 to 31, 33 to 40, 50 to 53, 56, 57 and 60 to 65 are rejected under 35 USC §103(a) as allegedly unpatentable over Apajalahti in view of Greiner. Various claims stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting, as discussed below.

Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for Claim Amendments

Support for the amended claims can be found throughout the application for the skilled artisan. For example, support for claims directed to feeds comprising an *E. coli* phytase in

recombinant, synthetic or isolated form can be found, inter alia, in paragraphs [0046] to [0048], [0080] and [0217] of U.S. patent application publication no. 20030049815 ("the '815 publication").

Information Disclosure Statement

Applicants thank the Examiner for noting that the references cited in the submitted EPO search reports need to be separately listed on FORM PTO/SB/O8A and 08B forms to be cited on the face of any patent issuing from this application; as discussed in paragraph 1, pages 2 to 3, of the OA. The appropriate forms are enclosed herein.

Specification

Regarding hyperlinks improperly embedded in the specification as filed, please see Applicants' amendment of October 18, 2005, addressing this issue; as discussed in paragraph 2, page 3, of the OA..

Priority

Applicants thank the Examiner for finding that SEQ ID NO:2 was disclosed in the first filed priority document USSN 08/910,798, filed August 13, 1997 (now USPN 5,876,997); as discussed in paragraph 3, pages 3 to 4, of the OA.

Issues under 35 U.S.C. §112, second paragraph

Claims 8 to 11, 19, 23 to 28, 30, 31, 33 to 41, 46, 48, 50 to 53, 56, 57, 64, 67, 68, 71 and 72 stand rejected as allegedly failing to comply with the requirements of 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, as set forth in detail in paragraphs 6 to 9, of the OA, pages 4 to 6. The instant amendment addresses these issues.

Issues under 35 U.S.C. §112, first paragraph

The rejection of claims 8 to 11, 19, 23 to 28, 30, 31, 33 to 41, 46, 48, 50 to 53, 56, 57 and 64, under section 112, first paragraph, is maintained, as set forth in detail in paragraphs 10 to 15, of the OA, pages 6 to 7. In particular, it is alleged, inter alia, that the claims are directed to any phytase encoded by a recombinant *E. coli* cell.

The instant amendment addresses this issue; the claims as amended clarify that the *E. coli* phytases used in the claimed compositions of the invention do not encompass an open-ended genus of any phytase encoded by a recombinant *E. coli* cell.

In light of the above remarks and the present claim amendments, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §103(a)

Cheng in view of Greiner

A *prima facie* case of obviousness has not been made

Claims 8 to 11, 13, 19, 23 to 28, 30, 31, 33 to 40, 50 to 53, 56, 57 and 64 remain rejected, and claims 67 and 68 are newly rejected, under 35 USC §103(a) as allegedly unpatentable over Cheng, et al., U.S. Patent No. 5,939,303, filed November 6, 1996, issued August 17, 1999 (hereinafter "Cheng"), in view of Greiner et al. (1993) Archives of Biochemistry and Biophysics 303:107-113 (hereinafter "Greiner"), as discussed in detail in paragraphs 18 to 22, pages 7 to 9, of the OA.

The Office acknowledges that Cheng does not teach an *E. coli* phytase in a food or feed; see, e.g., page 8, lines 5 to 6, of paragraph 6, of the OA.

Applicants also have respectfully submitted that Greiner does note cure this defect in Cheng because it does not teach use of *E. coli* phytase in a feed or food. The Office disagrees, and maintains that this limitation is taught by Greiner (see, e.g., page 8, lines 6 to 7, of paragraph 6, of the OA). The section of Greiner at issue is page 107, right-hand column:

> Phytases are of interest for biotechnological applications, especially for the reduction of phytate in food and feedstuff. Supplementation of animal feedstuff with phytases will increase the bioavailability of phosphate, thus decreasing phosphorus pollution in areas of intensive animal agriculture. The addition of phytases will diminish antinutritional effects of food having a high content of phytate. We have purified and characterized two phytases from *E. coli* cells grown in the late stationary phase.

While Greiner makes a general statement that phytases are useful for the reduction of phytate in food and feedstuffs, it does not specifically teach use of *E. coli* phytase in a feed or food. While Greiner characterizes two *E. coli* phytases having an activity optimum at an acidic pH, it does

not teach or suggest using an *E. coli* phytase in a food or a feed. Notably, while Cheng teaches use of various bacterial phytases in food or a feed, it does not suggest using an *E. coli* phytase in a food or a feed. In Cheng, while *E. coli* was used as a high performance expression system for all the non- *E. coli* phytases described therein, Cheng significantly does not include *E. coli* as a source of phytase for a food or a feed. Accordingly, Greiner does not cure the defect in Cheng.

Thus, because the combination of Chen and Greiner do not teach the instant claimed invention comprising foods or feeds comprising an *E. coli* phytase or methods of making and/or using same, a *prima facie* case of obviousness has not been made and the rejection under section 103(a) can be properly withdrawn.

The rejection is rebutted by secondary indicia of nonobviousness

Applicants respectfully aver that by submission of evidence of secondary indicia of nonobviousness they can overcome an obviousness rejection, even if, *arguendo*, the Patent Office has showed sufficient evidence of *prima facie* obviousness.

> The secondary considerations are also essential components of the obviousness determination. See In re Emert, 124 F.3d 1458, 1462, 44 USPQ2d 1149, 1153 (Fed. Cir. 1997) ("Without Emert providing rebuttal evidence, this *prima facie* case of obviousness must stand."). This objective evidence of nonobviousness includes **copying**, **long felt but unsolved need**, failure of others, see Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966), **commercial success**, see In re Huang, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 1689-90 (Fed. Cir. 1996), unexpected results created by the claimed invention, unexpected properties of the claimed invention, see In re Mayne, 104 F.3d 1339, 1342, 41 USPQ2d 1451, 1454 (Fed. Cir. 1997); In re Woodruff, 919 F.2d 1575, 1578, 16 USPQ2d 1934, 1936-37 (Fed. Cir. 1990), licenses showing industry respect for the invention, see Arkie Lures, Inc. v. Gene Larew Tackle, Inc., 119 F.3d 953, 957, 43 USPQ2d 1294, 1297 (Fed. Cir. 1997); Pentec, Inc. v. Graphic Controls Corp., 776 F.2d 309, 316, 227 USPQ 766, 771 (Fed. Cir. 1985), and skepticism of skilled artisans before the invention, see In re Dow Chem. Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1532 (Fed. Cir. 1988).

In re Rouffet, 47 U.S.P.Q.2D (BNA) at 1456.

Commercial success – long felt need - copying

Applicants submitted sufficient evidence of secondary indicia of nonobviousness to rebut any possible *prima facie* case by submission of the declaration of Dr. Nelson Barton, a research and development scientist at Diversa Corporation (the owner of this application), with their last

response. While Applicants reiterate and expressly incorporate by reference all previous arguments, including their last response with Dr. Barton's Rule 132 declaration; to briefly summarize:

Dr. Barton declared that he believes that at the time of this invention there was a long-felt need in the food, agricultural feed and biotech industry for an invention such as that set forth in the pending claims, i.e., an invention comprising use of an *E. coli* phytase in a food or a feed. Dr. Barton declared that this long-felt need is evidenced by the commercial success of Diversa Corporation's PHYZYME® *E. coli* phytase feed enzyme, noting that Diversa Corporation was the first entity to make and market an *E. coli* phytase-comprising feed (in collaboration with its exclusive licensee; in the U.S. PHYZYME® phytase is available for sale through Danisco Animal Nutrition, Danisco A/S, Copenhagen, Denmark).

Dr. Barton declared that use of an *E. coli* phytase is at least in part responsible for the commercial success of the claimed feed and food supplement (the "nexus") – because *E. coli* phytases have unique properties that distinguish them from phytases from other organisms, including other bacteria, they would be a better phytase enzyme to use in a food or feed.

Dr. Barton declares that after the priority date of this application, other food and feed enzyme companies realized the value of this discovery and began to investigate the use *E. coli* phytases in feeds, and summarizes that it was this invention that for the first time used an *E. coli* phytase in a food or feed to result in a better phytase enzyme-supplemented product, for which there was a long-felt need at the time of the invention.

The Office disagreed that the declaration provided sufficient secondary evidence to overcome a *prima facie* case of obviousness because, inter alia, one of the characteristics of the *E. coli* phytase that made it successful in a food or feed, i.e., its high activity in acidic conditions, was well known in the art; see page 9 of the OA.

Applicants respectfully note that that they are not trying claim any *E. coli* phytase already known in the art, including any *E. coli* phytase known to have activity under acidic conditions, but rather are claiming a composition that is described for the first time in this application – a food or feed comprising an *E. coli* phytase. Applicants respectfully aver that recognition that a property (high activity in acidic conditions) of one component of a multi-component, novel composition is not sufficient for the Office to disregard an expert declaration setting forth secondary evidence of

nonobviousness that includes copying, commercial success and long-felt need. This invention for the first time describes feeds or foods comprising an *E. coli* phytase. Applicants also submit that there is a sufficient nexus between the novelty of their new compounds (feeds and foods) and the secondary indicia of nonobviousness – the copying, commercial success and long-felt need of these feeds and foods.

Teaching away and difficulties in manufacturing phytase

The (amended) claimed invention encompasses feeds and foods comprising a phytase made by a method comprising providing a phytase-encoding nucleic acid isolated from an *E. coli*, or a synthetic or recombinant form of the phytase-encoding nucleic acid isolated from the *E. coli*, and expressing the nucleic acid under conditions which allow expression of the phytase. One of the unmet challenges in the industry before this invention was to economically provide sufficient quantities of isolated, synthetic or recombinant forms of phytase for the enzyme's inclusion in a feed or a food.

Before this invention it had been known that crude preparations of *E. coli* – lysed and dried and/or lyophilized cultured *E. coli* cells (the *E. coli* was initially isolated from chicken fecal matter) – when fed to phosphorus deficient growing chicks allowed normal growth and bone development; see e.g. Warden, et al. (1962) "Action of antibiotics in stimulating growth of poultry. Effect of *E. coli* and fecal preparations," Poultry Sci. 41:725 (hereinafter "Warden", submitted in the supplementary IDS attached herein). Warden suggested that the active agent "essentially increasing the phosphorus content of the ration" in the crude *E. coli* whole cell lysates fed to the growing chicks might be enzymatic in nature, e.g., a phytase or similar enzymes ("In these studies, the results suggest the probability that dried *E. coli* cellular material may contain phytase or similar enzymes making previously unavailable phosphorus available to the bird. Basis for this explanation is the fact that birds responded in a similar manner to addition of available phosphorus, or to one percent of lysed *E. coli*, which did not essentially increase the phosphorus content of the ration. This suggests that the effect … may be enzymatic in nature" (please see page 730, right hand column, of Warden).

However, before this invention no one had produced sufficient quantities of isolated, synthetic or recombinant forms of phytase for inclusion in a food or a feed, particularly an

economically viable commercial feed or food (see also Nelson, et al., (1971) "Effect of supplemental [*Aspergillus*] phytase on the utilization of phytate phosphorus by chicks; also submitted in the supplementary IDS attached herein).

As recently as 1996 (before the priority date of the instant application) experts in this field expressly dismissed bacteria as a source of phytase for use in a food or feed, see e.g., the review by Wodzinski and Ullah (1996) "Phytase" Advances in Applied Microbiol. 42:263-302 (hereinafter "Wodzinski") (also submitted in the supplementary IDS attached herein), in particular – page 272, section B, entitled "Bacterial Sources":

> Phytase has been detected in *Aerobacter aerogenes* ..., *Bacillus subtilis* ..., *Escherichia coli* ..., *Pseudomonas* ... . The only bacterial organism that produces extracellular phytase is B. subtilis. When phytase is produced by bacteria, the yields are low and the pH optimum is neutral to alkaline that precludes their use as feed additives. [emphasis added]

Thus, according to Wodzinski, as of 1996, experts in this field believed that when phytase is produced by bacteria – because the yields are low and the pH optimum is neutral to alkaline – use of an *E. coli* phytase as a feed additive is precluded.

Wodzinski provides a very detailed history of how difficult and costly it was to develop a fungal phytase for use in a food or feed (note: use of *E. coli* phytases was dismissed as impractical). For example, Wodzinski on page 264, lines 1 to 3 states: "[c]ommercialization [of phytase] was not possible until methods were available to develop and produce high yields of the enzyme in microbial culture or in plants." On page 266, section 3, Wodzinski states: "[t]he first concentrated effort to make phytase a commercial product started in 1962 ... in which approximately 12 man years were expended on the project." In brief, over 2000 organisms were screened for phytase activity, and an *A. niger* phytase was identified. Wodzinski concludes "[u]nfortunately, the yields of phytase at this time were not high enough to produce a product that would have to be increased, by one estimate, by about 250-fold just to break even" (please see the last paragraph of section 3, page 267).

Wodzinski also notes that in one effort it took 16 man years to isolate, characterize and sequence phytases made by an *A. niger* (please see the paragraph spanning pages 267 and 268, in section 4); and another group expended 40 man years to improve the yields of an *A. niger* (see the

first sentence of section 5, page 268); and concluded that the full effort took about 68 man years (see the sentence spanning pages 268 and 269).

Wodzinski's detailed history of how difficult and costly it was to develop a fungal phytase for use in a food or feed further evidences the need in the industry to identify a phytase suitable for use in a feed or food, and also evidences the need in the industry to develop a means to economically make a microbial phytase in sufficient amounts for inclusion in a food or feed.

Golovan, et al. (2000) Can. J. Microbio. 46:59-71 (hereinafter "Golovan") (also submitted in the supplementary IDS attached herein), provides additional evidence that there was a long-felt need in the industry to identify a phytase suitable for use in a feed or food. Golovan published about two and a half years after the filing date of this application's priority document, which is August 13, 1997, for USSN 08/910,798, which issued on March 2, 1999, as USPN 5,876,997 (this application published as U.S. patent app. pub. no. 20030049815, on March 13, 2003). Thus, Golovan published their work having the benefit of this invention's specification.

As is made clear in their introduction (page 60), Golovan was motivated to do the work described in this paper to address the long-felt need in the industry to identify and characterize a phytase suitable for use in a feed or food. After giving a brief history of *E. coli* phytase research, Golovan concludes with "[t]he purpose of this investigation was to reexamine the catalytic properties of the acid phosphatase [a phytase] from *E. coli*, and to overproduce the enzyme for further biological and structural studies and to determine its suitability for industrial applications." Thus, Golovan illustrates that even two and a half years after the priority date of this application the public state of the art (at least as far as the scientific literature) was still searching for an appropriate phytase for use in foods or feeds (Golovan probably wasn't aware of any patent publications, including USPN 5,876,997 (not surprising for an academic at that time) – they certainly didn't cite Applicants' patent or any other patent in their extensive list of references, please note pages 69 to 71, of Golovan).

In conclusion, Applicants have provided objective evidence of nonobviousness, including long-felt need, copying and commercial success of the claimed food or feed. Applicants respectfully aver that this objective evidence of nonobviousness is sufficient to rebut a possible *prima facie* case of obviousness.

In view of the above remarks, referenced publications and the evidence of secondary indicia of nonobviousness as set forth in Dr. Barton's expert declaration, Applicants submit that a *prima facie* case of obviousness has not been made, and alternatively, that they have rebutted any possible *prima facie* case of nonobviousness. Accordingly, the rejection under 35 U.S.C. §103(a) can be properly withdrawn.

Obviousness-like double patenting

USPN 6,110,719

Claims 8 to 14, 19, 20, 23, 26 to 31, 33 to 41, 44, 46, 50 to 55 and 60 to 66 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 6 to 7 of U.S. Patent No. (USPN) 6,110,719, issued from 09/259,214, (one of several priority documents to the instant application), because – although they are not identical – they are not patentably distinct from each other (see paragraphs 38 to 40, page 16, of the OA).

While Applicants respectfully traverse, only to expedite prosecution of this application to address this provisional rejection an appropriate Terminal Disclaimer addressing this issue is attached.

USPN 6,110,719 in view of Cheng

Claims 21, 22, 24, 25, 47 to 49 and 56 to 58, stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 6 to 7 of U.S. Patent No. (USPN) 6,110,719, in view of Cheng, because – although they are not identical – they are not patentably distinct from each other (see paragraphs 41 to 43, page 16, of the OA).

While Applicants respectfully traverse, only to expedite prosecution of this application to address this provisional rejection an appropriate Terminal Disclaimer addressing this issue is attached.

USSN 10/601,319

Claims 8 to 14, 19 to 31, 33 to 41, 44, 46, 48, 49 and 50 to 66, stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable

over claims 5, 23 to 28, 30, 31 and 40 to 49, of co-pending U.S. Patent Application No. (USSN) 10/601,319 (U.S. patent application publication no. 20040091968), because – although they are not identical – they are not patentably distinct from each other (see paragraphs 44 to 46, page 17, of the OA).

While Applicants respectfully traverse, only to expedite prosecution of this application to address this provisional rejection an appropriate Terminal Disclaimer addressing this issue is attached.

USSN 10/933,115

Claims 8 to 14, 19, 20, 23, 24, 26 to 31, 33 to 41, 44, 46, 48, 49 and 50 to 66, stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1 to 15, of co-pending U.S. Patent Application No. (USSN) 10/933,115 (unpublished), because – although they are not identical – they are not patentably distinct from each other (see paragraphs 47 to 49, page 17, of the OA).

While Applicants respectfully traverse, only to expedite prosecution of this application to address this provisional rejection an appropriate Terminal Disclaimer addressing this issue is attached.

USSN 11/056,354

Claims 8 to 14, 19, 20, 23, 26 to 31, 33 to 41, 44, 46, 50 to 55 and 60 to 66, stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 88, 89, and 96 to 103, of co-pending U.S. Patent Application No. (USSN) 11/056,354 (unpublished), because – although they are not identical – they are not patentably distinct from each other (see paragraphs 50 to 52, page 18, of the OA).

While Applicants respectfully traverse, only to expedite prosecution of this application to address this provisional rejection an appropriate Terminal Disclaimer addressing this issue is attached.

USSN 11/056,354 in view of Cheng

Claims 21, 22, 24, 25, 48, 49 and 56 to 58, stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 88, 89, and 96 to 103, of co-pending U.S. Patent Application No. (USSN) 11/056,354, in view of Cheng, because – although they are not identical – they are not patentably distinct from each other (see paragraphs 53 to 54, pages 18 to 19, of the OA).

While Applicants respectfully traverse, only to expedite prosecution of this application to address this provisional rejection an appropriate Terminal Disclaimer addressing this issue is attached.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs; 35 U.S.C. §103, and the obviousness-type double patenting rejections. In view of the above, claims in this application after entry of the instant amendment are believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket No. 564462001811. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at 858 720 5133.

Dated: April 5, 2007

Respectfully submitted,

By_/Gregory P. Einhorn/_____

Gregory P. Einhorn
Registration No.: 38,440
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
direct dial 858 720 5133
general office 858 720 5100
fax direct 858 523 5933
fax office 858 720 5125
email geinhorn@mofo.com